Pergamon

Tetrahedron, Vol. 53, No. 11, pp. 4035-4050, 1997

0040-4020/97 $17.00 + 0.00

PII: S0040-4020(97)00016-1

Synthesis of 1-Methyl-2-diphenylphosphino-3-(1'-isoquinolyl)indole; an Easily Racemised Ligand giving Insights into Catalytic Asymmetric Allylation§

Timothy D. W. Claridge, James M. Long, and John M.Brown*
The Dyson Perrins Laboratory, University of Oxford, South Parks Road, Oxford, OX1 3QY, U.K.

David Hibbs and Michael B. Hursthouse
School of Chemistry and Applied Chemistry, University of Wales College of Cardiff, P.O. Box 912, Cardiff CF1 3TB, U.K.

Abstract : The synthesis of the title compound is described, involving 2-lithiation and phosphinylation of the coupled heterocycle in the final step. Attempts to resolve the phosphine by previously described methods led to its immediate racemisation, also observed more slowly in the $PdCl_2$ complex, for which the X-ray structure is described. The phosphinamine formed a cationic Pd(1,3-diphenylallyl) complex with high diastereoselectivity. By analysis of the solution stucture using NMR techniques, in comparison with the X-ray structure, some inferences about the mechanism of allylic alkylation with related heterotopic ligands can be drawn. © 1997 Elsevier Science Ltd. All rights reserved.

Introduction.

In a previous paper[1] we described the synthesis and resolution of the atropisomerically chiral ligand 2-diphenylphosphino-1-(1'-isoquinolyl)naphthalene **1** (QUINAP). Since this and its relatives showed promising selectivity in catalytic asymmetric hydroboration[2] and allylic alkylation,[3] and at the same time there has been an upsurge of interest in the application of P-N and related heterotopic ligands in catalysis,[4] further work was encouraged. The X-ray structure of several Pd complexes of the parent compound reveals a consistent N-Pd-P bite angle of between 82° and 85° but an equally consistent distortion of the N-Pd vector out of the isoquinoline ring plane by around 25°, presumably as the best way of accommodating strain inherent in the chelate.

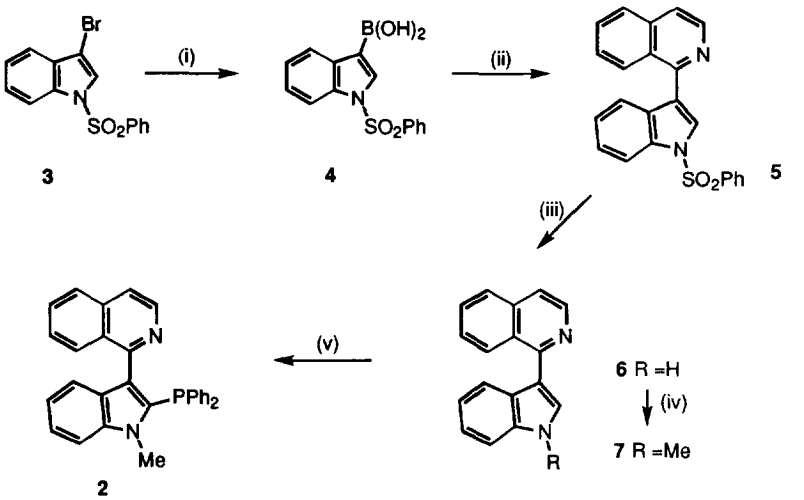
The basic ligand structure affords the opportunity for systematic study of the effects of changing parameters on enantioselectivity, including the electronic and steric character of both nitrogen[5] and phosphorus. In addition, variation of the ring size either of the isoquinoline (e.g. modifying to a benzpyrazole) or of the naphthalene (e.g. modifying to an indole) should permit some appraisal of the effects on reactivity and selectivity of varying the bite angle. It is the latter system which is of present concern, and a route to the ligand was established in which a key step was the direct metallation of the indole 2-position employing n-BuLi/KO-tBu, and phosphinylation of the organometallic reagent. Although readily synthesised, the parent compound **2** is prone to rapid racemisation, severely limiting its utility as a ligand. Even the $PdCl_2$ complex is stereolabile. Despite this, we have been able to prepare a 1,3-diphenylallylpalladium complex which exists essentially as a single diastereoisomer (>96%), and whose solid-state and solution structure are mechanistically revealing. The results are discussed in the context of asymmetric allylic alkylation.

---

§ This paper is dedicated to the memory of Arthur Birch, (Ph. D. supervisor of JMB) who made a distinguished contribution to the research record of the Dyson Perrins Laboratory between 1938 and 1949 at the begining of his career.

Ligand Synthesis

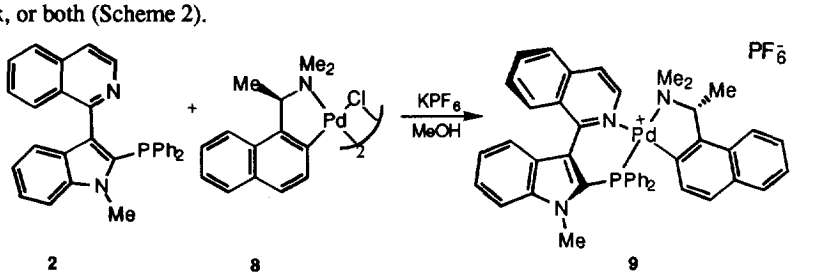
The preparation of compound **2** proved to be relatively straightforward as shown in Scheme 1, utilising the acidity of the indole 2-position which makes it the preferred site of lithiation.[6] The biaryl 3-(1'-isoquinolyl)-1-methylindole was synthesised by modification of a literature method for 3-arylation of indole which required the preparation of 1-phenylsulfonylindole-3-boronic acid; the 3-lithio derivative, which is its immediate precursor, is stable only at -100°C and at higher temperatures rearranges to the 2-isomer.[7] Coupling of the boronic acid with 1-chloroisoquinoline[8] proved to be straightforward and followed previous protocols. After deprotection and N-methylation, the key phosphinylation step was optimally carried out by using Schlosser's base,[9] which gave t-$BuOPPh_2$ as a by-product. This was separated from the desired product simply by washing the crude solid material with Et_2O.



Scheme 1. (i) t-BuLi, thf, -100°C; $B(OMe)_3$; HCl, H_2O; 41%; (ii) 1-chloroisoquinoline, $Pd(PPh_3)_4$, Na_2CO_3; DME, MeOH, 84%; (iii) NaOH, MeOH; reflux; 95%; (iv) NaH, thf; MeI; 94%; (v) n-BuLi, pentane, t-BuOK, thf; $ClPPh_2$, thf; 85%.

Attempted Resolution of Ligand 2

In previous work, we had demonstrated the effectiveness of the palladocycle derived from R- or S-dimethyl-1-naphthylethylamine as a resolving agent for the QUINAP class of ligands.[10] In the present case the phosphine was reacted with an equivalent of this palladium complex in MeOH for 2 h followed by precipitation of the product by adddition of KPF_6. The pale-green product was isolated, and revealed by ^{31}P NMR to be a single diastereomer on the basis of the singlet observed at 25.8 ppm; this was corroborated by the coherent set of aromatic resonances observed by ^1H NMR. Since the isolated yield was 99%, it was apparent that both hands of the ligand were able to form the same product, consistent only with a racemisation either of the phosphinamine or its Pd complex, or both (Scheme 2).



Scheme 2. Preparation of a single diastereomer of complex **9** by an asymmetric transformation of the first kind.

The configuration of complex **9** was determined by X-ray analysis of a crystal grown from pentane/$CHCl_3$. Full details are recorded in the Experimental Section. As expected on the basis of the earlier studies, the R,S-diastereomer is the one formed and hence is the more stable isomer. Its structure is shown in Figure 1, and has some features in common with the naphthylphosphine analogues discussed previously, but also some distinct features. Specifically, the chelate ring appears to be less strained, with the palladium almost in the plane of the isoquinoline ring, in contrast to the distortion seen in all other X-ray structures of QUINAP-type ligands which puts the nitrogen lone pair vector about 25° out of the ring plane. Some strain is evident, however, in the Cγ-N-Pd angle of 127°, and in the bending of the Cα-P bond out of the indole ring plane by 11°. In addition, the biaryl twist angle is somewhat smaller than in the naphthyl series, at 47° rather than in the 60-65° range, as previously observed.

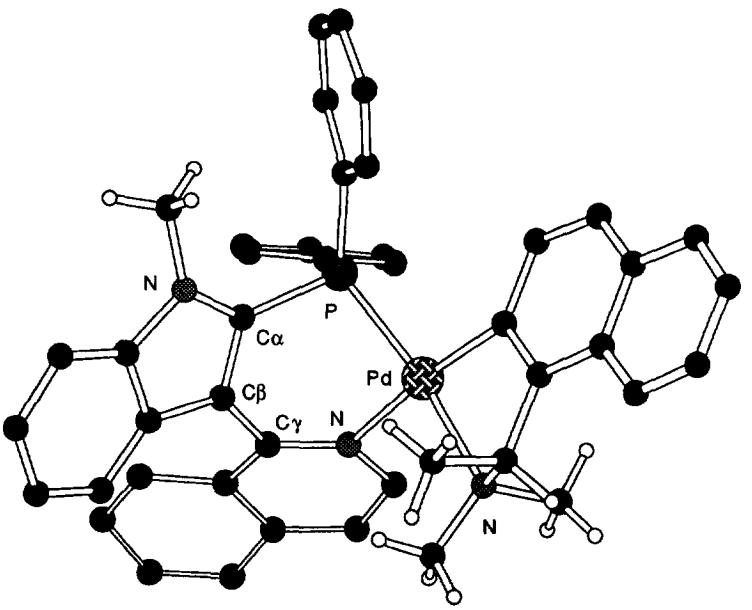


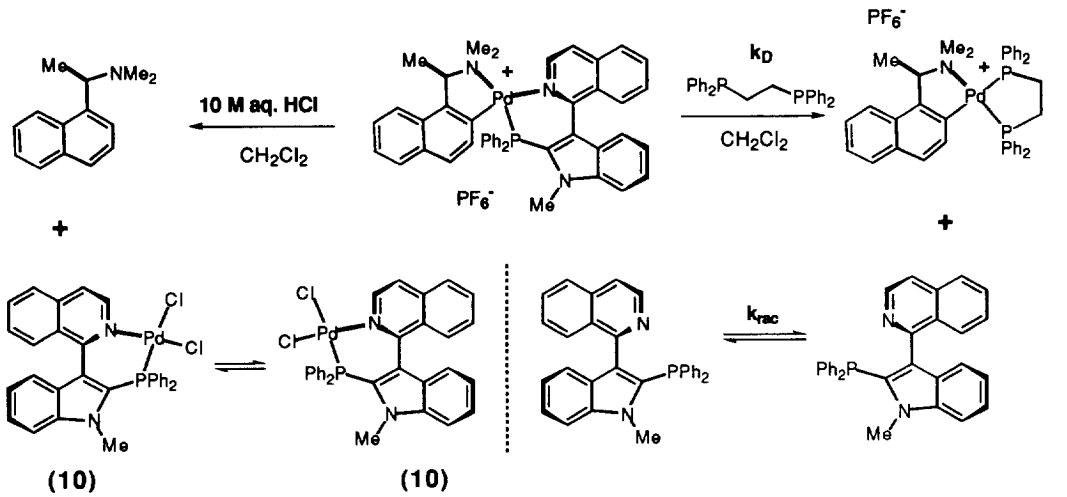
*Figure 1. Crystal structure of the R,S-isomer of complex **9**. Aromatic H-atoms and the counterion PF_6^- are omitted for clarity.*

Main bond lengths, angles and torsion angles [Å, °,°] :

P-Pd	2.256
N-Pd	2.136
P-Pd-N	82.4
Cα-P-Pd	98.6
Cβ-Cα-P	119.0
Cγ-Cβ-Cα	124.2
N-Cγ-Cβ	117.0
Pd-N-Cγ	127.4
P-Cα-Cβ-Cγ	-11.0
Cα-Cβ-Cγ-N	46.6
Cβ-Cγ-N-Pd	-4.0
Cγ-N-Pd-P	-46.8
N-Pd-P-Cα	60.8
Pd-P-Cα-Cβ	-49.9

The ligand can be released from complex **9** in two ways,[11] either by treatment with HCl to form the $PdCl_2$ complex **10**, or alternatively by treatment with 1,2-diphenylphosphinoethane (dppe) which releases the free ligand. Both of these procedures were carried out with polarimetric monitoring, which revealed the stereochemical lability of both ligand **2** and complex **10**. For the reaction with dppe, the changes in rotation with time depend on the concentration of dppe. At low concentration, the rate-limiting step is displacement, and reaction rate measured by the change in rotation is consistent with second-order kinetics with a first half-life of approximately 500 s. With a sixfold excess of dppe, the reaction is much more rapid ($t_{1/2}$ = ca. 100 s) and first-order in complex **9**. Now the rate-determining stage appears to be racemisation of the ligand. On this basis it is clear that the new phosphinamine is stereochemically labile at ambient temperature, precluding its use as a ligand in asymmetric catalysis. Addition of conc. aqueous HCl to complex **9** led to rapid formation of the corresponding $PdCl_2$ complex (as confirmed by ^{31}P NMR). It is of interest that the rotation decayed very rapidly in the first 60 s following acid addition, and then changed more slowly, implying an intermediate species. Over time the rotation

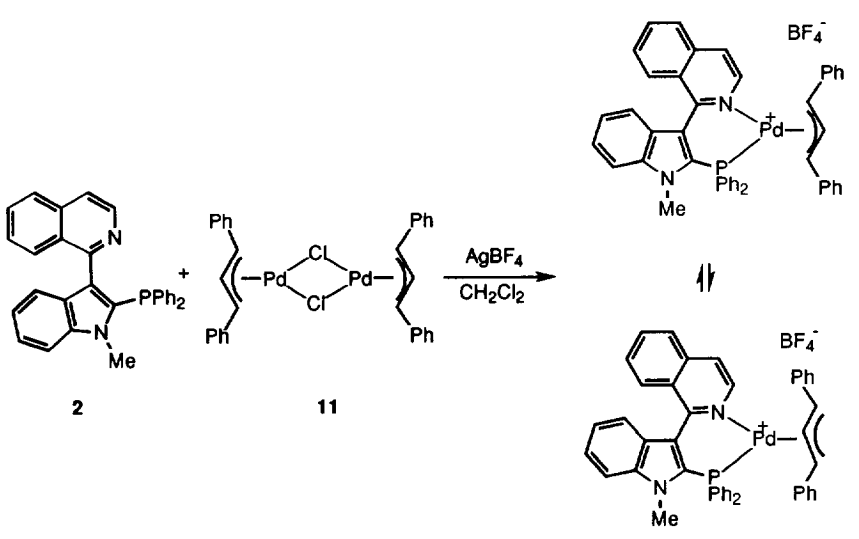
decayed almost to zero, consistent with racemisation of the complex. The process was much slower than for the free ligand, with a half-life of ca. 5000 s during the exponential decay phase, indicating that dissociation or part-dissociation is required before atropisomerism. These experiments are summarised in Scheme 3.



Scheme 3. Racemisation pathways for the free ligand 2 and its $PdCl_2$ complex.

Chemistry of the 1,3-diphenylallyl complex.

From the free ligand, the corresponding 1,3-diphenylallyl complex was prepared as a cationic tetrafluoroborate by the previously described route.[12] This was isolated as a 30:1 mixture of two racemic diastereomers (Scheme 4). For a given hand of the ligand, palladium can bind to either prostereogenic face of the 1,3-diphenylallyl group. It proved possible to grow X-ray quality crystals, assumed to be of the major component, from $CHCl_3$/pentane.



Scheme 4. Synthesis of the 1,3-diphenylallyl complex **12**.

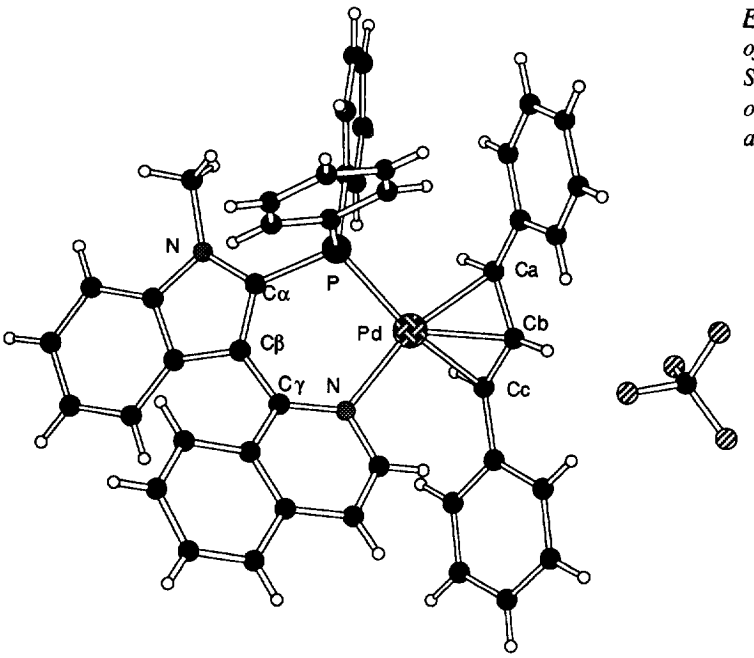


Figure 2. X-ray crystal structure of the diphenylallyl complex 12. Solvent molecules are omitted.Main bond lengths, angles and torsion angles [Å, °,°]

P-Pd	2.296
N-Pd	2.140
Cc-Pd	2.157
Cb-Pd	2.172
Ca-Pd	2.302
P-Pd-N	94.1
Cα-P-Pd	103.7
Cβ-Cα-P	123.6
Cγ-Cβ-Cα	129.4
N-Cγ-Cβ	120.6
Pd-N-Cγ	125.5
P-Cα-Cβ-Cγ	6.9
Cα-Cβ-Cγ-N	-45.3
Cβ-Cγ-N-Pd	26.0
Cγ-N-Pd-P	13.4
N-Pd-P-Cα	-36.0
Pd-P-Cα-Cβ	35.0

The structure and conformation of the chelate ligand in this diphenylallyl Pd-complex is very different from that seen in the related complex **9**. Most strikingly, the chelate bite angle is now 94° rather than 82°. The difference is achieved by several small compensating changes of bond angle in the chelate, the net result of which is that the nitrogen lone pair vector is no longer in the ring plane; the angle of 26° between the ideal vector and the Pd-N bond is very similar to that seen in a variety of QUINAP complexes and their relatives. Overall, the chelate is flatter in the allyl complex **12** than in the naphthylethylamine complex **9**, although the biaryl twist torsion angle remains similar at 46°. Comparison of the two structures reveals a conformational flexibility which was not previously recognised, and which must be important in control of the reagent and reactant coordination processes for asymmetric catalysis. The chelate geometry of the two complexes is compared in Figure 3, where **A** is derived from resolution complex **9** and **B** is derived from diphenylallyl **12**. Complex **9** is a single enantiomer, but complex **12** is racemic, being shown as the R-enantiomer in Figure 3. For comparison, the diphenylallyl complex **13** discussed by Helmchen and co-workers[13] is shown as **C** in a similar projection; this also brings out the much flatter orientation of the diphenylphosphino-oxazoline compared to the isoquinoline series. It is interesting to speculate that the different catalytic character of the two P-N chelate series (for example, the oxazoline-derived ligands are superior for allylic alkylations but inferior for catalytic hydroborations) is linked to the different geometries of the topologically similar chelate rings.

The most striking feature of the structure of the allyl complex lies in the coordination geometry of the allyl group. This is effectively twisted such that the Cc-Cb bond is in the P-Pd-N plane (torsion angle P-Pd-Cb-Cc = -14.5°) in contrast to the Ca-Cb bond (torsion angle N-Pd-Cb-Ca = 53°). In addition, the Cc-Pd bond length of 2.157 Å is significantly shorter than the Ca-Pd bond length of 2.302 Å.

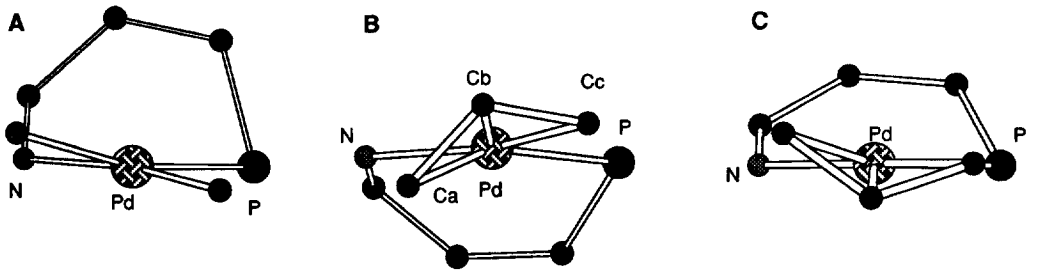
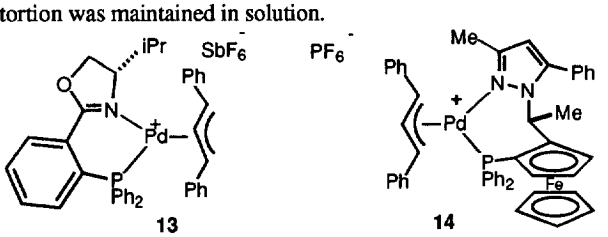


Figure 3. The chelate rings and directly coordinated atoms of complexes **10**, **12** and **13**.

Such twisting of a heterotopic chelate π-allyl had been observed previously, [14] although the present example represents a fairly extreme case. For example, the diphenylphosphino-oxazoline derived complex **13** prepared and analysed by Helmchen and co-workers has related torsion angles of P-Pd-C-C = 28.2° and N-Pd-C-C = -46.2°; the bond length variation is concomitantly less marked.[15] Since the ground-state geometry is of considerable interest in relation to the pathway for allylic alkylation (vide infra) attempts were made to determine whether the observed distortion was maintained in solution.



The proton and carbon 1D NMR spectra of the diphenylallyl complex **12** are fully described in the Experimental Section, and the first task was a complete assignment. It exists as >95% of a single diastereomer in solution, unlike the QUINAP derived analogue where a solvent-dependent equilibrium between the two E,E-isomers was observed which was observable on the NMR time-scale. To this end several convergent approaches were used. Firstly a full set of proton assignments was made. The aromatic region of the spectrum was quite well dispersed and immediate assignment of all phosphorus coupled protons (ortho- and meta- in PPh_2 and Ha of the allyl) was obtained through a $^1H\{^{31}P\}$ inverse-gated GARP decoupling experiment (Figure 4). Phase-sensitive DQF-COSY experiments, supported by nOe data, then identified the four separate phenyl rings, the four contiguous protons of the indole and the four protons of the carbocyclic ring of the isoquinoline, as well as the two protons H3' and H4' of the heterocyclic ring with their distinctively low coupling constant of 6 Hz.[16] They were distinguished through the additional long-range coupling of H8' to H4'. As is seen in the major diastereomer of the corresponding QUINAP complex, H3' is strongly shifted to low-frequency (1.3 ppm with respect to the free ligand) as a result of the ring-current shielding it experiences from the nearer Ph group of the allyl. Further distinction arises from double pulsed-field-gradient spin-echo (DPFGSE) transient nOe experiments,[17] which link the N-methyl protons to the indole H7, and to both P-Ph ortho-protons. There was a striking broadening of the ortho- and meta protons of one of the P-Ph rings, indicating restricted rotation. Examination of the X-ray structure indicates that the N-methyl group sits under one ring, and the nOe's are consistent with this being the one experiencing frozen rotation. The nOe's from the N-methyl to the broad ortho-protons could not be established in conventinal 1D nOe difference or in 2D ROESY experiments, but were quite apparent in the DPFGSE nOe by virtue of the very clean spectra afforded by this experiment.

The diphenylallyl group was assigned starting with the characteristic trans-coupling of Ha to P, and the rest followed from 2D ROESY and DQF-COSY experiments. In the ^{13}C NMR spectrum, the two terminal signals are widely dispersed, with the one trans to P coupled to it (22 Hz), comparable to related structures.[18] The dynamics of the allyl fragment were revealed by a 2D ^1H ROESY experiment (500 ms mixing time). This defined the corresponding signals associated with the minor diastereomer, present to 3%. Whilst the terminal allyl protons of

the major species are well dispersed at 6.23 ppm (Ha) and 4.20 ppm (Hc), in the minor species they overlap at 5.6 ppm. The vicinal coupling constants are similar in the two species, and this together with the fact that the interconversion takes place within the time-scale of spin relaxation, indicates that the minor species is the alternative E,E rather than an E,Z-diastereomer. The mechanism of interconversion is as demonstrated before, since Ha is dynamically linked to Hc', and Hc to Ha'.[19]

Overall the solution structure appears similar to that observed in the crystal, but the question remains as to whether the observed distortion of the allyl moiety pertains in solution. All the evidence indicates that it does, and a symmetrical species with Ha and Hc in the P-Pd-N plane was created as a Chem 3D model using the X-ray parameters as a starting point. Measurement of close interproton contacts makes two predictions for this structure - that the isoquinoline proton H3' should be close to the allyl proton Ha such that a strong nOe is anticipated, and that Hm1 should be very close to He. In practice there is a barely observable nOe between H3' and Ha, and none between Hm1 and He. In contrast, predictions based on the distances observed in the X-ray are borne out, specifically the shorter contact between H3' and Hg than between H3' and Ha, and the specific interaction of Hd with one pair of P-Ph ortho-protons only. We conclude that the structure is the same in solution and the crystal. Recent work by Togni, Pregosin and their colleagues provides similar conclusions about the allylic complex **14**, and also about a related P,S ligated palladium allyl complex.[20]

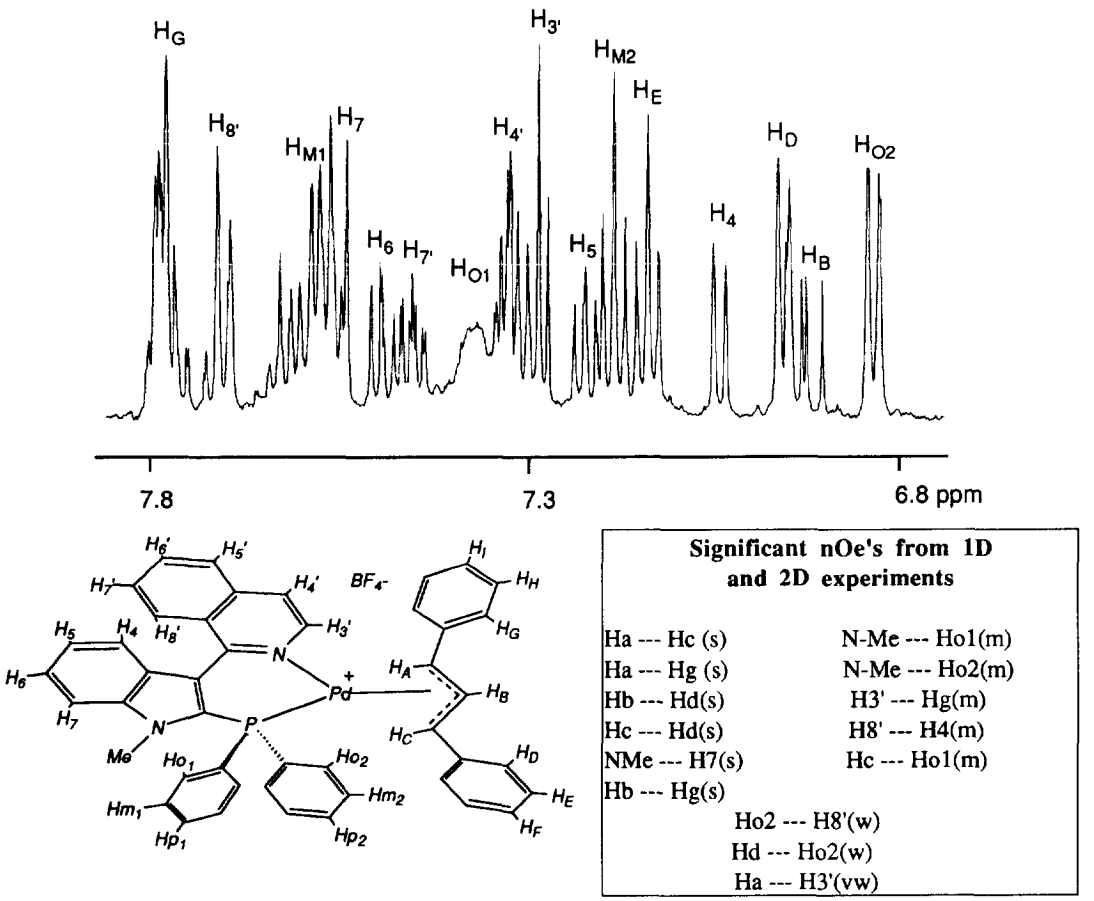


Figure 4. ^{31}P decoupled ^{1}H NMR spectrum of the diphenylallyl complex **12**, recorded as described in the text and demonstrating the high degree of dispersion of the aromatic region. Note the broadened signal of H_{O1} due to the observed restricted rotation. Significant non-ortho intracomplex nOe's are recorded in the inset.

Asymmetric Allylic Alkylation with P-N ligands:

Of all transition-metal complex catalysed reactions of synthetic interest, allylic alkylation has the most transparent mechanism, because the critical bond-forming step occurs outside the coordination sphere.[21] This has led to a considerable effort to define the pathway for this step, including molecular mechanics calculations.[22] In an early paper on the asymmetric variant, Bosnich and co-workers suggested that the transition-state resembled the ground state, basing this on the observation that the major diastereomer of palladium allyl in their case was the one leading to the preferred product.[23] A counter argument was presented by Pfaltz who suggested that a product-like geometry (i.e. the η^2-coordinated alkene formed by addition to the allyl terminus) would help to explain the high stereoselectivities observed for Pd-catalysed allylic alkylation of 1,3-diphenylallyl acetate with his oxazoline-derived ligands which significantly exceeded that predicted on the basis of the diastereomeric ratio of the Pd allyls.[24] In the QUINAP series there is little ground state discrimination between the two diastereomeric allyls and yet under appropriate conditions the e.e. is high. In order to rationalise this we considered the reaction to occur through a late transition state, with the new C-C bond significantly formed, and also predicted alkylation to be preferred trans- to phosphorus.

Discussion of a reaction pathway where many coordinates change in terms of being "early" or "late" is in any case an oversimplification, since the various changes do not necessarily occur in concert. Aside from the energy changes associated with reactant approach as the new C-C bond to the incoming nucleophile is formed, the significant parameters include (**a**) rehybridisation of the reacting carbon atoms of the nucleophile, (**b**) rehybridisation of the reacting carbon of the allyl and (**c**) reorientation of the allyl so that the remaining two carbons form the bound alkene of the immediate product. In the ground state of complex **12**, which now appears to be typical of P-N ligated palladium allyls, much of the reorientation required by (**c**) has already occurred, and is associated with unusually high diastereoselectivity (30 : 1). By itself, this does not inform us on how far C-C bond formation will have progressed at the transition-state; indeed the energy surface may be rather flat because of the compensating gains of intrinsic bonding energy and losses due to increased steric interaction. On balance, we prefer to interpret the body of current evidence in terms of a substantial degree of C-C bond development at the transition-state.

Acknowledgements. We thank EPSRC and BP for a CASE Studentship (to JML) for which we appreciate useful discussions with Dr. Evert Ditzel and Dr. Neil Cooley. Mrs. E. McGuinness was extremely helpful in the obtention of NMR spectra. Johnson-Matthey kindly provided a loan of $PdCl_2$.

Experimental

General. NMR spectra were recorded on a Varian Gemini 200, Bruker AC 200, Bruker AM 250, or Bruker AM 500 spectrometer. ^1H chemical shifts are reported in δ ppm relative to $CHCl_3$ (7.27 ppm), ^{13}C chemical shifts are reported relative to the central peak of $CDCl_3$ (77.0 ppm), and ^{31}P chemical shifts are reported relative to 85% aqueous phosphoric acid (0.0 ppm). Elemental microanalyses were carried out using a Carlo Erba 1106 elemental analyser. Mass spectra were recorded on a BIO-Q spectrometer. IR spectra were recorded on a Perkin Elmer 1750 FT spectrometer. Optical rotations were recorded on a Perkin Elmer 241 polarimeter. Melting points were recorded on a Reichert-Kofler block, and are uncorrected. Solvents were dried immediately before use by distillation from standard drying agents. Sodium tetrafluoroborate, potassium acetate (BDH), silver tetrafluoroborate, dimethyl malonate, N,O-bis(trimethylsilyl)acetamide, 15-crown-5 and Eu(hfc)$_3$ (Aldrich Chemical Co.) were commercially available. di-μ-chloro-bis(1,3-diphenyl-π-allyl)dipalladium[12] and cis-[(R)-dimethyl(1-(1-naphthyl)ethyl)aminato-C^2,N]-[(S)-1-(2-diphenylphosphino-1-naphthyl)isoquinoline] palladium (II) hexafluorophosphate[1] were prepared according to literature procedures.

(1-Benzenesulphonyl)-1H-Indole-3-Boronic acid 4. (3-Bromo-1-benzenesulphonyl)-1H-indole (22.8 g, 68 mmol) was dissolved in THF (500ml) and the solution was cooled to -100 °C (Et_2O / dry ice / $N_{2(l)}$). *t*BuLi (80 ml, 136 mmol) was added as quickly as possible, keeping the internal temperature below -80 °C via addition of extra liquid nitrogen. The mixture was stirred for 5 mins and trimethylborate (9.63 ml, 85 mmol) was added neat and the solution allowed to warm to room temperature overnight. 3M HCl (125 ml) was added carefully and the solution was stirred for 10 minutes. The resulting solution was then extracted with CH_2Cl_2 (2 x 250 ml). The combined organic layers were washed with 2M NaOH (3 x 200 ml). The aqueous portions were acidified and extracted with CH_2Cl_2 (3 x 150 ml). The organic extracts were dried ($MgSO_4$) and the solvent was removed *in vacuo* to give the boronic acid (8.40 g, 41 %) as a brown solid. No further purification was carried out.

(3-(1'-Isoquinolyl)-1-Benzenesulphonyl)-1H-Indole 5. 1-Chloroisoquinoline (3.27 g, 20 mmol) was added as a solid to a solution of tetrakis(triphenylphosphine)palladium (0) (1.0 g, 1 mmol) in DME (100 ml), and stirred for 10 minutes under an argon atmosphere to give a yellow/green solution. (1-Benzenesulphonyl)-1H-indole-3-boronic acid (6.0 g, 20 mmol) in the minimum amount of methanol was added to give a yellow solution. Sodium carbonate solution (20 ml, 2M) was added and the solution refluxed overnight (16 h). The red reaction mixture was allowed to cool, and the solid was filtered off. The solid was washed with CH_2Cl_2 until it was white. The filtrate was removed *in vacuo* to give a brown oil. The oil was dissolved in CH_2Cl_2 (600 ml), washed with saturated brine (2 x 300 ml), dried ($MgSO_4$), and the solvent removed *in vacuo* to give a brown viscous oil. Et_2O (75 ml) was added and a brown solid formed. Recrystallisation from CH_2Cl_2 gave (3-(1'-isoquinolyl)-1-benzenesulphonyl)-1H-indole (6.5g, 84%), as a white powder, m.p. 180-182 °C. HRMS, mass calc. = 385.101075, mass found = 385.101152 (-0.2 ppm). ^{1}H NMR (500 MHz): δ ($CDCl_3$) 8.66 (1H, d, J = 5.6 Hz, $H_{3'}$), 8.26 (1H, dd, J = 8.5, 0.9 Hz, $H_{8'}$), 8.14 (1H, dd, J = 8.1, 1.1 Hz, $H_{5'}$), 8.03 (1H, s, H_2), 8.00 (2H, dd, J = 7.5, 1.3 Hz, H_o), 7.93 (1H, dd, J = 8.1, 0.6 Hz, H_7), 7.78 (1H, dd, J = 7.7, 0.9 Hz, H_4), 7.76 (1H, dt, J = 8.4, 0.9 Hz, $H_{6'}$), 7.69 (1H, d, J = 5.6 Hz, $H_{4'}$), 7.61 (1H, ddd, J = 8.5, 8.4, 1.1 Hz, $H_{7'}$), 7.58 (1H, tt, J = 7.7, 1.3 Hz, H_p), 7.48 (2H, dd, J = 7.7, 7.5 Hz, H_m), 7.43 (1H, ddd, J = 8.1, 7.8, 0.9 Hz, H_6), 7.31 (1H, ddd, J = 7.8, 7.7, 0.6 Hz, H_5); ^{13}C NMR (125.8 MHz): δ ($CDCl_3$) 153.6 ($C_{1'}$), 152.6 ($C_{3'}$), 138.5 (C_{ipso}), 137.3 ($C_{10'}$), 135.5 (C_8), 134.5 (C_{para}), 130.8 ($C_{6'}$), 130.7 (C_9), 129.8 (C_{meta}), 128.0 ($C_{8'}$), 127.8 ($C_{9'}$), 127.6 ($C_{5'}$), 127.4 (C_{ortho}), 127.3 ($C_{7'}$), 127.0 (C_2), 125.7 (C_5), 124.4 ($C_{4'}$), 122.1 (C_4), 121.7 (C_3), 120.5 (C_6), 113.9 (C_7); ν_{max} (KBr) 1622 (m) (Ar-H), 1594 (m) (Ar-H), 1510 (m) (Ar-H), 1264 (s) (C-O), 1250 (s) (C-O), 826 (m) (Ar-H), 812 (m) (Ar-H), and 747 (m) (Ar-H) cm^{-1}. m/z (DCI, NH_4^+) 385 (78%, M+H), 245 (100%, M-SO_2Ph).

3-(1'-Isoquinolyl)-1H-Indole 6. (3-(1'-Isoquinolyl)-1-benzenesulphonyl)-1H-indole (4.0 g, 10 mmol) was dissolved in MeOH (30 ml) and NaOH solution (2N, 6 ml) was added and the solution refluxed for two hours. The solution was cooled and the product was extracted with CH_2Cl_2 (3 x 20 ml). The combined organic layers were washed with water (40 ml) and brine (40 ml), dried ($MgSO_4$) and filtered. The solvent was removed *in vacuo* to give a brown oil. The oil was dissolved in a little CH_2Cl_2 and Et_2O (100 ml) was added to give a light brown powder of 3-(1'-isoquinolyl)-1H-indole (2.31 g, 95 %), m.p. 204-206 °C. Analysis: $C_{17}H_{12}N_2$ requires C, 83.58; H, 4.95; Found C, 83.68; H, 4.83. ^{1}H NMR (500 MHz): δ ($CDCl_3$) 9.10 (1H, br s, N-H), 8.65 (1H, d, J = 5.7 Hz, $H_{3'}$), 8.30 (1H, dd, J = 8.5, 1.0 Hz, $H_{8'}$), 7.89 (1H, dd, J = 8.2, 1.0 Hz, $H_{5'}$), 7.80 (1H, dd, J = 7.9, 1.0 Hz, H_4), 7.71 (1H, dt, J = 8.2, 1.0 Hz, $H_{6'}$), 7.63 (1H, d, J = 5.7 Hz, $H_{4'}$), 7.57 (1H, s, H_2), 7.53 (1H, ddd, J = 8.5, 8.2, 1.0 Hz, $H_{7'}$), 7.43 (1H, dd, J = 8.1, 0.8 Hz, H_7), 7.26 (1H, ddd, J = 8.1, 7.9, 1.0 Hz, H_6), 7.18 (1H, dt, J = 7.9, 0.8 Hz, H_5); ^{13}C NMR (125.8 MHz): δ ($CDCl_3$) 156.2 ($C_{1'}$), 142.6 ($C_{3'}$), 137.3 ($C_{10'}$), 136.7 (C_8), 130.4 ($C_{6'}$), 128.3 ($C_{8'}$), 127.8 ($C_{9'}$), 127.5 (C_9), 127.4 ($C_{7'}$), 127.3 ($C_{5'}$), 126.3 (C_2), 123.0 (C_5), 121.3 ($C_{4'}$), 121.0 (C_4), 119.3 (C_6), 116.4 (C_3), 111.8 (C_7); λ_{max} (MeOH) 343 (ε/dm^3 mol^{-1} cm^{-1} = 8 320), 280 (ε/dm^3 mol^{-1} cm^{-1} = 9 190) nm; ν_{max} (KBr) 3138 (s) (Ar-H), 1618 (m) (C=N), 1552 (s) (C=C), 1510 (m) (Ar-H), 1436 (s) 1236 (s) cm^{-1}; m/z (CI^+, NH_4^+) 262 (6%, M+NH_4^+), 245 (100%, M+H^+).

(3-(1'-Isoquinolyl)-1-Methyl)-1H-Indole 7. Sodium hydride (15 mmol, 360 mg, 60% dispersion in oil) was placed in a preweighed schlenk, washed with pentane (3 x 50 ml) and dried *in vacuo* . The clean solid was

suspended in THF (60 ml) and 3-(1'-isoquinolyl)-1H-indole (3.0 g, 12.3 mmol) in THF (60 ml) was added slowly at 0 °C. The solution was stirred for 1 hour. MeI (0.81 ml, 13 mmol) was then added neat and the solution stirred for a further 4 hours at 0 °C. The reaction was quenched with sat. $NaHCO_3$ (120 ml) and the organics were extracted with CH_2Cl_2 (3 x 80 ml). The combined organics were dried ($MgSO_4$), filtered and the solvent was removed *in vacuo* to give a yellow oil. The oil was dissolved in a small amount of CH_2Cl_2 and Et_2O (100 ml) was added to give (3-(1'-isoquinolyl)-1-methyl)-1H-indole (2.98 g, 94 %) as a yellow powder, m.p. 184-185 °C. ^{1}H NMR (500 MHz): δ ($CDCl_3$) 8.63 (1H, d, J = 5.6 Hz, $H_{3'}$), 8.40 (1H, dd, J = 8.4, 1.0 Hz, $H_{8'}$), 7.88 (1H, dd, J = 8.2, 1.1 Hz, $H_{5'}$), 7.81 (1H, dd, J = 8.0, 0.7 Hz, H_4), 7.69 (1H, dt, J = 8.2, 1.0 Hz, $H_{6'}$), 7.59 (1H, d, J = 5.6 Hz, $H_{4'}$), 7.57 (1H, s, H_2), 7.54 (1H, ddd, J = 8.4, 8.2, 1.1 Hz, $H_{7'}$), 7.44 (1H, dd, J = 8.2, 0.6 Hz, H_7), 7.33 (1H, ddd, J = 8.2, 8.0, 0.7 Hz, H_6), 7.20 (1H, dt, J = 8.0, 0.6 Hz, H_5), 3.93 (3H, s, N-Me); ^{13}C NMR (125.8 MHz): δ ($CDCl_3$) 156.0 ($C_{1'}$), 143.0 ($C_{3'}$), 137.5 ($C_{10'}$), 137.3 (C_8), 130.7 ($C_{6'}$), 130.2 (C_2), 128.4 ($C_{8'}$), 128.0 ($C_{9'}$), 127.7 (C_9), 127.3 ($C_{7'}$), 127.2 ($C_{5'}$), 122.6 (C_5), 121.6 ($C_{4'}$), 120.9 (C_4), 119.0 (C_6), 115.4 (C_3), 109.9 (C_7), 34.2 (N-Me); ν_{max} (KBr) 3138 (s) (Ar-H), 1618 (m) (C=N), 1552 (s) (C=C), 1510 (m) (Ar-H), 1436 (s) 1236 (s) cm^{-1}; m/z (CI^+, NH_4^+) 262 (6%, $M+NH_4^+$), 245 (100%, $M+H^+$).

(3-(1'-Isoquinolyl)-2-Diphenylphosphino-1-Methyl)-1H-Indole 2. (3-(1'-Isoquinolyl)-1-methyl)-1H-indole (1.29 g, 5 mmol) was dissolved in THF (20 ml) and *n*BuLi (3.12 ml, 5.5 mmol) in pentane (30 ml) was added slowly with rapid stirring at -10 °C. The solution was then cooled to -90 °C and *t*BuOK (590 mg, 5.25 mmol) in THF (20 ml) was added slowly over 15 minutes, keeping the temperature below -80 °C. The solution was raised to -60 °C and PPh_2Cl (2.0 ml, 10.5 mmol) in THF (10 ml) was added with rapid stirring. The solution was raised to room temperature over several hours and the mixture stirred overnight. The solution was quenched with sat. $NaHCO_3$ (80 ml) and extracted with CH_2Cl_2 (3 x 80 ml). The combined organic layers were washed with water (80 ml), brine (80 ml), dried ($MgSO_4$), filtered and the solvent was removed *in vacuo* to give a brown oil. The oil was washed with Et_2O (100 ml) to give a brown powder of (3-(1'-isoquinolyl)-2-diphenylphosphino-1-methyl)-1H-indole (1.87g, 85%), m.p. 203-205 °C. HRMS, mass calc. = 443.167712, mass found = 443.168399 (-1.5 ppm). ^{1}H NMR (500 MHz): δ ($CDCl_3$) 8.54 (1H, d, J = 5.7 Hz, $H_{3'}$), 7.83 (1H, d, J = 8.4 Hz, $H_{8'}$), 7.78 (1H, d, J = 8.2 Hz, $H_{5'}$), 7.62 (1H, dd, J = 8.3, 8.2 Hz, $H_{6'}$), 7.57 (2H, ddd, J = 8.7, 7.4, 2.1 Hz, H_{o1}), 7.53 (1H, d, J = 5.7 Hz, $H_{4'}$), 7.46 (1H, d, J = 8.4 Hz, H_7), 7.38-7.31 (5H, m, H_6, $H_{7'}$, H_{m1}, H_{p1}), 7.27 (1H, d, J = 8.0 Hz, H_4), 7.22 (2H, ddd, J = 8.7, 7.6, 2.3 Hz, H_{o2}), 7.12 (1H, dd, J = 8.0, 7.9 Hz, H_5), 6.99 (3H, m, H_{m2}, H_{p2}), 3.72 (3H, s, N-Me); ^{13}C NMR (125.8 MHz): δ ($CDCl_3$) 156.1 ($C_{1'}$), 142.1 ($C_{3'}$), 139.1 (C_8), 135.9 (C_2), 134.3 (C_{i1}, J = 7.2 Hz), 133.8 (C_{i2}, J = 6.8 Hz), 133.1 (C_{o1}, J = 19.5 Hz), 132.5 ($C_{10'}$), 132.3 (C_{o2}, J = 19.1 Hz), 129.5 ($C_{6'}$), 128.9 ($C_{9'}$), 128.6 (C_9), 128.5 (C_{p1}), 128.4 (C_{m1}, J = 6.4 Hz), 128.1 ($C_{8'}$), 127.7 (C_{p2}), 127.6 (C_{m2}, J = 7.0 Hz), 126.4 ($C_{5'}$), 126.3 ($C_{7'}$), 125.3 (C_3, J = 16.9 Hz), 123.2 (C_6), 120.2 (C_4), 120.0 (C_5), 119.6 ($C_{4'}$), 109.2 (C_7), 32.1 (N-Me, J = 9.5 Hz); ^{31}P NMR (101.3 MHz): δ ($CDCl_3$) -26.4 (s, $-PPh_2$); ν_{max} (KBr) 3047 (s) (Ar-H), 2925 (w) (C-H), 1619 (m) (C=N), 1557 (s) (C=C), 1432 (s) (P-Ph), 1312 (s), 826 (s), 746 (s), 693 (s) cm^{-1}; m/z (APCI$^+$, NH_3) 460 (10%, $M+NH_4^+$), 459 (100%, $M+O+H^+$), 443 (82%, $M+H^+$).

(S,R)-cis-[Dimethyl(1-(1-Naphthyl)Ethyl)Aminato-*C*$_2$,*N*]-[(3-(1'-Isoquinolyl)-2-Diphenyl phosphino-1-Methyl)-1H-Indole] Palladium (II) Hexafluorophosphate 9. (+)-Di-μ-chloro*bis*[(R)-dimethyl(1-(1-naphthyl)ethyl)aminato-*C*$_2$,*N*] dipalladium (II) (768 mg, 1.13 mmol) and (3-(1'-isoquinolyl)-2-diphenylphosphino-1-methyl)-1H-indole (1.00 g, 2.26 mmol) were placed in a large Schlenk tube under argon. Degassed methanol (60 ml) was added *via* syringe and the mixture stirred for 2 hours to give a yellow solution. Potassium hexafluorophosphate (500 mg, 2.7 mmol) in water (60 ml) was added *via* syringe with vigorous stirring, and a yellow solid precipitated. The solution was stirred for a further hour when more water (100 ml) was added. The solid was collected by filtration, and washed with diethyl ether to give a single diastereomer of (R,S)-*cis*-[dimethyl(1-(1-naphthyl)ethyl)aminato-*C2*,*N*]-[(3-(1'-isoquinolyl)-2-diphenylphosphino-1-methyl)-1H-indole] palladium (II) hexafluorophosphate as a yellow solid (2.00 g, 99 %), m.p. 215-217 °C (decomposes

at 230 °C). $[\alpha]_D^{21}$ = -230 (c = 0.1, $CHCl_3$); ^1H NMR (500 MHz): δ ($CDCl_3$) 8.60 (1H, d, J = 6.2 Hz, $H_{3'}$), 8.02 (1H, d, J = 6.2 Hz), 7.88 (1H, d, J = 8.1, $H_{8'}$), 7.81 (1H, dd, J = 8.0, 0.7 Hz, H_4), 7.69 (1H, dt, J = 8.2, 1.0 Hz, $H_{7'}$), 7.59 (1H, d, J = 5.6 Hz, $H_{4'}$), 7.77 (1H, d, J = 8.6 Hz), 7.76-7.67 (5H, m), 7.53-7.45 (5H, m), 7.40 (1H, t, J = 7.4 Hz), 7.31-7.25 (9H, m), 7.01 (1H, d, J = 8.4 Hz), 6.58 (1H, dd, 8.3, 6.3 Hz), 4.43 (1H, quin, J = 6.0 Hz, H_α), , 3.20 (3H, s, N-Me), 2.90 (3H, d, J = 1.7 Hz, N-Me), 2.70 (3H, d, J = 3.3 Hz, N-Me), 2.00 (3H, d, J = 6.3 Hz, C-Me); ^{13}C NMR (125.8 MHz): δ ($CDCl_3$) 153.7 ($C_{1'}$), 150.5 (C_{nap}), 148.8 ($C_{10'}$), 141.0 (C_8, J = 4 Hz), 140.4 ($C_{3'}$), 136.8 (C_{nap}), 136.5 (C_{o1}, J = 12.0 Hz), 135.0 (C_{o2}, br m), 133.4 (C_{m1}, J = 14.9 Hz), 132.8 (C_{nap}), 132.4 (C_{p1}), 131.3 (C_{nap}), 129.4 (C_{m2}, J = 14.5 Hz), 129.3 ($C_{8'}$), 129.2 ($C_{9'}$), 128.7 ($C_{6'}$), 128.6 (C_{p2}), 128.4 (C_{nap}), 127.4 ($C_{7'}$), 126.8 (C_{i1}, J = 28.3 Hz), 126.7 (C_9), 126.5 (C_{nap}), 126.2 (C_6), 125.8 (C_{i2}, J = 32.0 Hz), 125.6 (C_{nap}), 125.5 (C_{nap}), 125.2 ($C_{5'}$), 124.7 (C_5), 124.6 (C_3, J = 14.9 Hz), 124.2 (C_{nap}), 123.8 (C_2, J = 52.5 Hz), 123.0 ($C_{4'}$), 122.4 (C_{nap}), 120.9 (C_4), 111.2 (C_7), 73.7 (CH), 51.6 (N-CH_3), 47.7 (N-CH_3), 33.6 (N-CH_3,indole), 24.3 (C-$\underline{CH_3}$); ^{31}P NMR (101.3 MHz): δ ($CDCl_3$) 25.8 (s, -PPh_2), -129.3 (heptet, J = 353 Hz, PF_6^-); vmax (KBr) 3051 (s) (Ar-H), 2880 (m) (C-H), 1622 (m) (C=N), 1557 (s) (C=C), 1438 (s) (P-Ph), 1312 (s), 846 (vs) (P-F), 746 (s), 693 (s) cm-1; m/z (electrospray) 746 (100%, M^+) with expected isotope pattern.

[(3-(1'-Isoquinolyl)-2-Diphenylphosphino-1-Methyl)-1H-Indole] Palladium (II) Dichloride 10. Concentrated hydrochloric acid (5 ml) was added to a solution of cis-[(R)-dimethyl(1-(1-naphthyl)ethyl)aminato-*C2,N*]-[(3-(1'-isoquinolyl)-2-diphenylphosphino-1-methyl)-1H-indole] palladium (II) hexafluorophosphate (374 mg, 0.42 mmol) in CH_2Cl_2 (5 ml) and the mixture stirred for 2 hours. The solvent was removed *in vacuo* to leave an orange solid. The solid was dissolved in CH_2Cl_2 (20 ml) then washed with water (20 ml), 10% hydrochloric acid (20 ml), water (20 ml) and saturated brine (20 ml). The solution was dried with $MgSO_4$ then the solvent removed *in vacuo* to give a yellow solid. Recrysallisation from CH_2Cl_2 gave [(3-(1'-isoquinolyl)-2-diphenylphosphino-1-methyl)-1H-indole] palladium (II) dichloride (214 mg, 83%) as a yellow crystals, m.p. 270 °C (decomposition occurs from 170 °C). ^1H NMR (500 MHz): δ ($CDCl_3$) 9.58 (1H, d, J = 6.7 Hz, $H_{3'}$), 7.88 (1H, d, J = 8.7 Hz, $H_{8'}$), 7.85 (1H, d, J = 8.1 Hz, $H_{5'}$), 7.81 (2H, ddd, J = 13.0, 7.8, 2.0 Hz, H_{o1}), 7.78 (1H, dd, J = 8.3, 8.1 Hz, $H_{6'}$), 7.72 (2H, br m, H_{o2}), 7.66 (1H, dt, J = 7.5, 1.0 Hz, H_{p2}), 7.63 (1H, d, J = 6.7 Hz, $H_{4'}$), 7.52 (2H, ddd, J = 7.5, 6.7, 2.8, H_{m2}), 7.50 (2H, m, H4, H_7), 7.48 (1H, dd, J = 8.7, 8.3 Hz, $H_{7'}$), 7.37 (1H, dt, J = 7.6, 2.0 Hz, H_{p1}), 7.26 (2H, ddd, J = 7.8, 7.6, 2.6 Hz, H_{m1}), 7.24 (1H, dd, J = 8.1, 7.8 Hz, H_5), 7.20 (1H, dd, J = 8.1, 7.9 Hz, H_6), 3.20 (3H, s, N-CH_3); ^{13}C NMR (62.9 MHz): δ ($CDCl_3$) 153.3 ($C_{1'}$), 146.4 ($C_{3'}$), 141.1(C_8), 136.7 ($C_{10'}$), 135.1 (C_{o2}, br m), 132.9 (C_{o1}, J = 12.8 Hz), 132.7 (C_{p2}), 132.4 ($C_{6'}$), 132.3 (C_{p1}), 129.1 (C_{m1}, J = 8.8 Hz), 129.1 ($C_{8'}$), 128.8 (C_{m2}, J = 12.4 Hz), 128.4 (C_3, J= 20.0 Hz), 128.1 ($C_{7'}$), 127.3 ($C_{9'}$, J = 7.0 Hz), 126.9 ($C_{5'}$), 126.1 (C_9), 125.6 (C_4), 125.5 (C_{i2}, J = 54.7 Hz), 123.6 (C_2, J = 63.0 Hz), 123.0 (C_{i1}, J = 53.8), 122.5 (C_5), 122.1 ($C_{4'}$), 121.6 (C_6), 111.0 (C_7), 33.4 (N-Me); ^{31}P NMR (101.3 MHz): δ ($CDCl_3$) 15.4 (s, P-Ph_2); ν_{max} (KBr) 3051 (m) (Ar-H), 1619 (m) (C=N), 1595 (m) (conj. C=C), 1436 (s) (P-Ph), 1100 (s), 821 (s), 746 (s) (Ar-H), 717 (s) (Ar-H) and 692 (s) (Ar-H) cm-1; m/z (electrospray) 583 (100%, M-Cl) with expected isotope pattern.

Decomplexation of cis-[(R)-Dimethyl(1-(1-Naphthyl)Ethyl)Aminato-C_2,*N*]-[(S)-(3-(1'-Isoquinolyl)-2-Diphenylphosphino-1-Methyl)-1H-Indole] Palladium (II) Hexafluorophosphate (1 equiv. of DPPE). cis-[(R)-Dimethyl(1-(1-naphthyl)ethyl)aminato-C_2,*N*]-[(S)-(3-(1'-isoquinolyl)-2-diphenylphosphino-1-methyl)-1H-indole] palladium (II) hexafluorophosphate (20 mg, 0.022 mmol) was placed in a 10 ml graduated flask and dissolved in CH_2Cl_2 (10 ml). A sample was taken out and an optical rotation was run. At a recorded time DPPE (9 mg, 0.022 mmol) was added as a solid and the solution stirred rapidly for 10 sec. A sample was taken out and placed in the polarimeter and readings were taken every 30 seconds from the initial addition of the DPPE, until no further change was seen in the reading. This experiment was repeated three times.

Decomplexation of cis-[(R)-Dimethyl(1-(1-Naphthyl)Ethyl)Aminato-C_2,N]-[(S)-(3-(1'-Isoquinolyl)-2-Diphenylphosphino-1-Methyl)-1H-Indole] Palladium (II) Hexafluorophosphate (6 equiv. of DPPE). cis-[(R)-Dimethyl(1-(1-naphthyl)ethyl)aminato-C_2,N]-[(S)-(3-(1'-isoquinolyl)-2-diphenylphosphino-1-methyl)-1H-indole] palladium (II) hexafluorophosphate (20 mg, 0.022 mmol) was placed in a 10 ml graduated flask and dissolved in CH_2Cl_2 (10 ml). A sample was taken out and an optical rotation was run. At a recorded time DPPE (54 mg, 0.132 mmol) was added as a solid and the solution stirred rapidly for 10 sec. A sample was taken out and placed in the polarimeter and readings were taken every 15 seconds from the initial addition of the DPPE, until no further change was seen in the reading. This experiment was repeated twice.

Racemisation of [(3-(1'-Isoquinolyl)-2-Diphenylphosphino-1-Methyl)-1H-Indole] Palladium (II) Dichloride. cis-[(R)-Dimethyl(1-(1-naphthyl)ethyl)aminato-C_2,N]-[(S)-(3-(1'-isoquinolyl)-2-diphenyl phosphino-1-methyl)-1H-indole] palladium (II) hexafluorophosphate (20 mg, 0.022 mmol) was placed in a 10 ml graduated flask and dissolved in CH_2Cl_2 (10 ml). A sample was taken out and an optical rotation was run. At a specified time conc. HCl (0.26 ml, 3 mmol) was added and the solution was stirred rapidly for 30 s. A sample was placed in the polarimeter and readings were taken every 1 min for the first 10 mins and then every 10 mins thereafter until no further change was seen in the optical rotation. This experiment was repeated twice more.

Decomplexation of (3-(1'-Isoquinolyl)-2-diphenylphosphino-1-methyl)-1H-Indole. 1,2-Bis(diphenylphosphino)ethane (1.67 g, 4.2 mmol) was added to a solution of cis-[(R)-Dimethyl(1-(1-naphthyl)ethyl)aminato-C_2,N]-[(S)-(3-(1'-Isoquinolyl)-2-diphenylphosphino-1-methyl)-1H-Indole]palladium (II) hexafluorophosphate (4.22 g, 4.2 mmol) in dichloromethane (50 ml). The solution was stirred for 2 hours then toluene (50 ml) added and the solvent removed *in vacuo* to leave a white solid. Toluene (100 ml) was added and the suspension stirred for 5 minutes. The solid was removed by filtration and washed with toluene (2 x 100 ml). The combined toluene extracts were reduced *in vacuo* to leave (+/-)-(3-(1'-Isoquinolyl)-2-diphenylphosphino-1-methyl)-1H-Indole (1.57 g, 86 %) as a white powder, m.p. 204-206 °C $[\alpha]_D^{21} = 0$ (c = 0.1, $CHCl_3$) .

[(3-(1'-Isoquinolyl)-2-Diphenylphosphino-1-Methyl)-1H-Indole]-[1,3-Diphenyl-π-allyl] Palladium (II) Tetrafluoroborate 12. Di-μ-chloro-bis(1,3-diphenyl-π-allyl) dipalladium (67.0 mg, 0.1 mmol), (3-(1'-isoquinolyl)-2-diphenylphosphino-1-methyl)-1H-indole (88 mg, 0.2 mmol) and silver tetrafluoroborate (78 mg, 0.4 mmol) were placed in a Schlenk tube under argon. Degassed CH_2Cl_2 (10 ml) was added *via* syringe to give an orange suspension which was stirred for 16 hours. The solid was removed by filtration, then the solution was concentrated *in vacuo* and Et_2O was added to precipitate a yellow solid. The solvent was removed *in vacuo* to give [(3-(1'-isoquinolyl)-2-diphenylphosphino-1-methyl)-1H-indole]-[1,3-diphenyl-π-allyl] palladium (II) tetrafluoroborate (92 %, 151 mg) as a brown powder in a diastereomeric ratio of 30:1, m.p. 215-217 °C (decomposes at 230 °C). ^{1}H NMR (500 MHz): δ (CD_2Cl_2) 7.76 (1H, dd, J = 8.1, 1.7 Hz, $H_{5'}$), 7.76 (2H, dd, J = 7.6, 1.6 Hz, H_G), 7.74 (1H, ddd, J = 8.4, 8.1, 1.1 Hz, $H_{6'}$), 7.68 (1H, tt, J = 8.1, 1.4 Hz, H_{P1}), 7.67 (1H, dd, J = 6.4, 1.1 Hz, $H_{8'}$), 7.59 (1H, tt, J = 7.4, 1.6 Hz, H_I), 7.56 (2H, br ddd, J = 8.1, 7.8, 2.4 Hz, H_{M1}), 7.53 (1H, dd, J = 7.0, 1.1 Hz, H_7), 7.53 (2H, dd, J = 7.6, 7.4 Hz, H_H), 7.46 (1H, ddd, J = 7.8, 7.0, 0.8 Hz, H_6), 7.42 (1H, ddd, J = 8.4, 6.4, 1.1 Hz, $H_{7'}$), 7.35 (2H, br m, H_{O1}), 7.29 (1H, tt, J = 7.9, 1.4, H_{P2}), 7.29 (1H, d, J = 6.3 Hz, $H_{4'}$), 7.26 (1H, tt, J = 7.8, 1.2 Hz, H_F), 7.24 (1H, dd, J = 6.3 Hz, $H_{3'}$), 7.18 (1H, ddd, J = 8.2, 7.8, 1.1 Hz, H_5), 7.14 (2H, ddd, J = 8.1, 7.9, 2.6 Hz, H_{M2}), 7.10 (2H, dd, J = 8.1, 7.8 Hz, H_E), 7.00 (1H, d, J = 8.2 Hz, H_4), 6.91 (2H, dd, J = 8.1, 1.2 Hz, H_D), 6.89 (1H, dd, J = 13.9, 10.8, H_B), 6.79 (2H, ddd, J = 12.6, 8.1, 1.4, H_{O2}), 6.23 (1H, dd, J = 13.9, 8.9 Hz, H_A), 4.20 (1H, d, J = 10.8 Hz, H_C), 3.20 (3H, s, N-Me); ^{13}C NMR (125.8 MHz): δ ($CDCl_3$) 156.0 ($C_{1'}$), 142.6 ($C_{3'}$), 141.4 (C_8, J = 3.4 Hz), 137.7 ($C_{10'}$), 137.4 (C_J), 134.6 (C_K, J = 5.4 Hz), 133.2 (C_{o2}, J = 13.6 Hz), 132.9 ($C_{6'}$), 132.8 (C_{o1}, J = 13.9 Hz), 132.4 (C_{p2}), 132.3 (C_{p1}), 130.8 (C_I), 130.5 (C_H), 130.2 (C_{m1}, J = 11.7 Hz), 129.8 (C_{m2}, J = 11.3 Hz), 129.6 ($C_{8'}$), 129.1 (C_E), 128.9 (C_G), 128.6 ($C_{7'}$), 128.5 ($C_{9'}$), 128.3 (C_F), 127.7 (C_D, J = 2.7 Hz), 127.5 (C_3, J = 46.9 Hz), 127.4 (C_9), 127.1 ($C_{5'}$), 126.5 (C_{i2}, J = 36.1 Hz), 126.2 (C_2, J = 58.6 Hz), 125.7 (C_6), 124.4 (C_{i1}, J = 39.0 Hz), 122.4 (C_5), 122.3 ($C_{4'}$), 121.6 (C_4), 111.6 (C_B, J = 5.1 Hz), 111.4 (C_7), 103.2 (C_A, J

= 22.1 Hz), 73.0 (C_C, J = 5.4 Hz), 34.2 ($N-CH_3$); ^{31}P NMR (101.3 MHz): δ ($CDCl_3$) 25.8 (s, $-PPh_2$); ν_{max} (KBr) 3046 (s) (Ar-H), 1621 (m) (C=N), 1550 (s) (C=C), 1491 (m), 1461 (m), 1437 (m) (P-Ph), 1318 (s), 1062 (vs) (B-F), 821 (s), 755 (s), 695 (s) cm^{-1}; m/z (electrospray) 828 (100%, M^+) with expected isotope pattern.

cis-[(R)-Dimethyl(1-(1-naphthyl)ethyl)aminato-C_2,N]-[(S)-(3-(1'-Isoquinolyl)-2-diphenylphosphino-1-methyl)-1H-Indole]palladium (II) Hexafluorophosphate; Crystals suitable for x-ray analysis were grown from a $CHCl_3$ / pentane mixture.

Empirical formula	C44H38F6N3P2Pd1
Formula weight	891.11
Temperature	120(2) K
Wavelength	0.71069 Å
Crystal system	Monoclinic
Space group	P2(1)
Unit cell dimensions	a = 8.461(2) Å, α = 90.000(8) deg. b = 21.737(6) Å, β = 95.040(8) deg. c = 10.968(3) Å, γ = 90.000(8) deg.
Volume	2009.4(9) $Å^3$
Z	2
Density (calculated)	1.473 mg/m^3
Absorption coefficient	.605 mm^{-1}
F(000)	906
Crystal size	0.22 x 0.16 x 0.13 mm
θ range for data collection	1.86 to 25.30 deg.
Index ranges	-9<=h<=6, -24<=k<=23, -12<=l<=12
Reflections collected	8465
Independent reflections	5177 [R(int) = 0.0891]
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	5177 / 1 / 479
Goodness-of-fit on F^2	1.033
Final R* indices (all data)	R_1 = 0.0624, ωR_2 = 0.1607
R* indices [for all data]	R_1 = 0.0716, ωR_2 = 0.1792
Absolute Structure Parameter	0.01(5)
Largest diff. peak and hole	1.142 and -0.996 e.$Å^{-3}$

* $R_1 = \Sigma||F_O|-|F_C|| / \Sigma|F_O|$, $\omega R_2 = \{\Sigma[\omega(F_O^2-F_C^2)^2] / \Sigma[\omega(F_O^2)^2]\}^{1/2}$ and $\omega = 1/[\sigma^2(F_O)^2]$

[(3-(1'-Isoquinolyl)-2-diphenylphosphino-1-methyl)-1H-indole]-[1,3-diphenyl-π-allyl] palladium (II) Tetrafluoroborate. Crystals suitable for x-ray crystal analysis were grown from a $CHCl_3$/pentane mixture.

Empirical formula	C46H38B1Cl2F4N2P1Pd1
Formula weight	913.86
Temperature	120(2) K
Wavelength	0.71069 Å
Crystal system	Triclinic
Space group	P-1
Unit cell dimensions	a = 11.041(3) Å, α = 80.46(2) deg. b = 13.259(4) Å, β = 70.00(2) deg. c = 15.066(2) Å, γ = 76.36(2) deg.
Volume	2005.3(8) $Å^3$
Z	2
Density (calculated)	1.513 mg/m^3
Absorption coefficient	.691 mm^{-1}
F(000)	928
Crystal size	0.25 x 0.16 x 0.18 mm
θ range for data collection	2.00 to 25.11 deg.
Index ranges	-10<=h<=12, -15<=k<=9, -7<=l<=17
Reflections collected	3640
Independent reflections	3420 [R(int) = 0.0618]
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	3420 / 6 / 515
Goodness-of-fit on F^2	0.949
Final R* indices (all data)	R_1 = 0.0444, ωR_2 = 0.1138
R* indices [for all data]	R_1 = 0.0500, ωR_2 = 0.1158
Largest diff. peak and hole	0.693 and -0.461 e.$Å^{-3}$

* $R_1 = \Sigma||F_o|-|F_c|| / \Sigma|F_o|$, $\omega R_2 = \{\Sigma[\omega(F_o^2-F_c^2)^2] / \Sigma[\omega(F_o^2)^2]\}^{1/2}$ and $\omega = 1/[\sigma^2(F_o)^2]$

NMR studies on [(3-(1'-Isoquinolyl)-2-Diphenylphosphino-1-Methyl)-1H-Indole]-[1,3-Diphenyl-π-allyl] Palladium (II) Tetrafluoroborate. Studies were performed on a Bruker AMX500 equipped with an inverse broadband z-axis gradient probe and with a static sample. ROESY spectra were recorded with a 500 ms 2.6 kHz continuous-wave spin-lock field. Data sets were collected with a 6 ppm spectral width as a 2K x 512W data set with 16 scans per increment, phase-sensitive detection in F1 via TPPI and were processed with phase-shifted sine-bells in both dimensions. DQF-COSY spectra were collected with a 3 ppm spectral width (the aromatic region) as a 1K x 256W data set, 8 scans per increment with TPPI, and were processed with phase-shifted sine-bells. 1D nOe difference spectra were recorded with 7 s presaturation applied with frequency cycling within each irradiated multiplet (100 x 70 ms) and with a composite 90° pulse to minimise SPT effects. DPFGSE-nOe spectra were obtained using a selective 25 ms Gaussian inversion pulse and with 1 ms gradients of approximately 5:5:8:8 G cm-1 in the gradient spin-echo sequences. Mixing times of 400 and 800 ms were used containing one pair of purge gradients of ca. 18:-18 G cm-1. The relaxation delay between scans was 4 s. 128 scans were collected for each spectrum, requiring only about 15 mins in each case.

References

1 Alcock, N. W.; Brown, J. M.; Hulmes, D. I. *Tetrahedron: Asymmetry* **1993**, *4*, 743-756.

2 Brown, J. M.; Hulmes, D. I.; Layzell, T. P. *J. Chem. Soc., Chem. Commun.* **1993**, 1673-1674; Valk, J. M.; Whitlock, G. A.; Layzell, T. P.; Brown, J. M. *Tetrahedron: Asymmetry* **1995**, *6*, 2593-2 596.

3 Brown, J. M.; Hulmes, D. I.; Guiry, P. J. *Tetrahedron* **1994**, *50*, 4493-4506.

4 Peer, M.; Dejong, J. C.; Kiefer, M.; Langer, T.; Rieck, H.; Schell, H.; Sennhenn, P.; Sprinz, J.; Steinhagen, H.; Wiese, B.; Helmchen, G. *Tetrahedron* **1996**, *52*, 7547-7583; and references therein.

5 Valk, J. M.; Claridge, T.; Brown, J. M.; Hibbs, D.; Hursthouse, M. B. *Tetrahedron: Asymmetry* **1995**, *6*, 2597-2610; Bayston, D. J., to be published

6 Shirley, D.A., Roussel, P.A. *J. Am. Chem. Soc.* **1952**, *74* 375-8.

7 Conway, S. C.; Gribble, G. W. *Heterocycles* **1990**, *30*, 627-633.

8 Ikehara, M. *Chem. Pharm. Bull.* **1954**, *2*, 111

9 Lochmann, L.; Popisil, J.; Lim, D. *Tetrahedron Lett.* **1966**, *7*, 257; Schlosser, M. J. *Organometal. Chem.* **1967**, *8*, 9.

10 Alcock, N. W.; Hulmes, D. I.; Brown, J. M. *J. Chem. Soc., Chem. Commun.* **1995**, 395-397.

11 For a recent discussion see : Dunina, V. V.; Golovan, E. B. *Tetrahedron: Asymmetry* **1995**, *6*, 2747-2754; Dunina, V. V.; Golovan, E. B.; Gulyukina, N. S.; Buyevich, A. V. *Tetrahedron: Asymmetry* **1995**, *6*, 2731-2746.

12 Togni, A.; Rihs, G.; Pregosin, P. S.; Ammann, C. *Helv. Chim. Acta* **1990**, *73*, 723-732.

13 Sprinz, J.; Kiefer, M.; Helmchen, G.; Huttner, G.; Walter, O.; Zsolnai, L.; Reggelin, M. *Tetrahedron Lett.* **1994**, *35*, 1523-1526.

14 ref 13 and also Togni, A.; Burckhardt, U.; Gramlich, V.; Pregosin, P. S.; Salzmann, R. *J. Am. Chem. Soc.* **1996**, *118*, 1031-1037.

15 We acknowledge assistance from the CSSR database at Daresbury: Allen, F.H.; Kennard, O. *Chemical Design Automation News*, **1993**, *8*, 31-37.

16 Batterham, T. J.; NMR Spectra of Simple Heterocycles", Wiley-Interscience, NY, (1973)

17 Stott, K., Stonehouse, J., Keeler, J., Hwang, T-L., and Shaka, A. J. *J. Am. Chem. Soc* **1995**, *117*, 4199-4200.

18 Malet, R.; Morenomanas, M.; Parella, T.; Pleixats, R. *J. Org. Chem.* **1996**, *61*, 758-763.

19 For recent discussions of allylpalladium dynamics see : ref. 3, and Breutel, C.; Pregosin, P. S.; Salzmann, R.; Togni, A. *J. Am. Chem. Soc.* **1994**, *116*, 4067-4068; Gogoll, A.; Ornebro, J.; Grennberg, H.; Backvall, J. E. *J. Am. Chem. Soc.* **1994**, *116*, 3631-3632; Granberg, K. L.; Backvall, J. E. *J. Am. Chem. Soc.* **1992**, *114*, 6858-6863.

20 Albinati, A.; Pregosin, P. S.; Wick, K. *Organometallics* **1996**, *15*, 2419-2421.

21 Trost, B. M.; VanVranken, D. L. *Chem. Rev.* **1996**, *96*, 395-422.

22 Penacabrera, E.; Norrby, P. O.; Sjogren, M.; Vitagliano, A.; Defelice, V.; Oslob, J.; Ishii, S.; O'Neill, D.; Akermark, B.; Helquist, P. *J. Am. Chem. Soc.* **1996**, *118*, 4299-4313; Norrby, P.-O.; Åkermark, B.; Hæffner, F.; Hansson, S.; Blomberg, M.*J. Am. Chem. Soc.* **1993**, *115*, 4859-4867.

23 (a) Auburn, P. R.; Mackenzie, P. B.; Bosnich, B. *J. Am. Chem. Soc.* **1985**, *107*, 2033-2046; (b) Mackenzie, P. B.; Whelan, J.; Bosnich, B. *J. Am. Chem. Soc.* **1985**, *107*, 2046-2054.

24 Pfaltz. A. *Acc. Chem. Res.* **1993**, *26*, 339-345; Vonmatt, P.; Lloyd-Jones, G. C.; Minidis, A.; Pfaltz, A.; Macko, L.; Neuburger, M.; Zehnder, M.; Ruegger, H.; Pregosin, P. S. *Helv. Chim. Acta* **1995**, *78*, 265-284.

(*Received in UK* 15 *October* 1996; *accepted* 8 *January* 1997)